Appendix A

1. (Amended) An endosomal lysing agent comprising a compound having one or more hydrolyzable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyls and wherein said compound is capable of effecting the lysis of an endosome in response to a change in pH.

2. The endosomal lysing agent of claim 1, comprising a biocompatible compound.

3. The endosomal lysing agent of claim 1, comprising a biodegradable compound.

4. The endosomal lysing agent of claim 1, comprising a biocompatible and biodegradable compound.

5. (Amended) An endosomal lysing agent comprising a compound having one or more hydrolyzable functional moieties and one or more ionizable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyl, and wherein said compound is capable of effecting the lysis of an endosome in response to a change in pH.

6. The endosomal lysing agent of claim 5, comprising a biocompatible compound.

7. The endosomal lysing agent of claim 5, comprising a biodegradable compound.

8. The endosomal lysing agent of claim 5, comprising a biocompatible and biodegradable compound.

9. The endosomal lysing agent of claim 1, 2, 3, 4, 5, 6, 7, or 8 comprised of a polymer.

10. The endosomal lysing agent of claim 9, wherein the hydrolysis of said one or more hydrolyzable functional moieties effects a hydrophobic/hydrophilic transition of said compound.

11. The endosomal lysing agent of claim 10, wherein said hydrolysis further effects the release of a compound capable of disrupting lipid bilayers.

12. The endosomal lysing agent of claim 5, wherein said one or more ionizable functional moieties comprises proton acceptor sites.

13. (Canceled)

14. (Amended) The endosomal lysing agent of claim 1 or 5, wherein each of said ortho-ester containing monomers is selected from the group consisting of N-[2-methyl-1,3-O-ethoxyethylidine-prpanediol]methacrylamide, ortho-ester derivatives of tartaric acid, ortho-ester derivatives of treitol, and ortho-ester derivatives of dithiothreitol.

15. The polymeric lysing agent of claim 9, wherein the polymeric lysing agent is combined in a form selected from the group consisting of:

mixed polymers;

linear co-polymers;

branched co-polymers; and

dendrimer branched co-polymers.

16. The lysing agent of claim 9, wherein said agent is further functionalized with a targeting agent selected from the group consisting of low density lipoproteins, transferrin, asiaglycoproteins, gp120 envelope protein of human immunodeficiency virus, antibodies and carbohydrates.

17. (Amended) A biocompatible composition comprising:

a packaging agent, characterized by an ability to bind to a therapeutic agent and mediate import into endosomes; and

a lysing agent comprising a compound having one or more hydrolyzable functional moieties

selected from the group consisting of ortho-esters, hydrazones, and cis-actonyl and wherein said compound is capable of effecting the lysis of an endosome in response to a change in pH.

18. The biocompatible composition of claim 17, wherein said compound further comprises one or more ionizable functional moieties.

19. The biocompatible composition of claim 17 or claim 18, wherein said composition comprises a polymer.

20. The biocompatible composition of claim 17 or 18, wherein said packaging agent and said lysing agent are combined in a form selected from the group consisting of:

mixed polymers;

linear co-polymers;

branched co-polymers; and

dendrimer branched co-polymers.

21. The biocompatible composition of claim 17 or claim 18, wherein said therapeutic agent comprises a nucleic acid.

22. The biocompatible composition of claim 17 or claim 18, wherein the packaging agent associates with the therapeutic agent through a covalent interaction.

23. The biocompatible composition of claim 17 or claim 18, wherein the packaging agent associates with the therapeutic agent through a non-covalent interaction.

24. The composition of claim 17 or claim 18, wherein the packaging agent condenses the nucleic acid.

25. The composition of claim 17 or claim 18, wherein the packaging agent condenses the nucleic acid to a size less than 150 nm.

26. The composition of claim 17 or claim 18, wherein the packaging agent comprises a material with high charge density.

27. The composition of claim 26, wherein said packaging agent comprises a tertiary amine or a quaternary amine.

28. The composition of claim 27, wherein said packaging agent is selected from the group consisting of 2-[dimethylamino]ethyl methacrylate, (3-aminopropyl)methacrylamide, 2-aminoethyl methacrylamide, aspartic acid, glutamic acid and polymers thereof.

29. The composition of claim 17 or claim 18, wherein the hydrolysis of said one or more hydrolyzable functional moieties effects a hydrophobic/hydrophilic transition of said compound.

30. The composition of claim 17 or claim 18, wherein said hydrolysis further effects the release of a compound capable of disrupting lipid bilayers.

31. The composition of claim 18, wherein said one or more ionizable functional moieties comprises proton acceptor sites.

32. (Amended) A cell delivery composition comprising:
a compound to be delivered to a cell;
a delivery agent bound to the compound; and
an endosomolytic agent of claim 1 or 5.

Q5 SUB B6)

33. (Canceled)

34. (Canceled)

35. The cell delivery composition of claim 32, wherein the compound to be delivered to a

cell is selected from the group consisting of anti-AIDS substances, anti-cancer substances, antibiotics, immunosuppressants, anti-viral substances, enzyme inhibitors, neurotoxins, opioids, hypnotics, antihistamines, lubricants, tranquilizers, anti-convulsants, muscle relaxants, anti-Parkinson substances, anti-spasmodics and muscle contractants, miotics, anti-cholinergics, anti-glaucoma compounds, anti-parasite compounds, anti-protozoal compounds, anti-hypertensives, analgesics, anti-pyretics, anti-inflammatory agents, local anesthetics, ophthalmics, prostaglandins, anti-depressants, anti-psychotic substances, anti-emetics, imaging agents, specific targeting agents, neurotransmitters, proteins, cell response modifiers, vaccines, anti-sense agents, RNA and ribozymes.

36. (Canceled)

37. (Canceled)

38. (Canceled)

39. (Amended) A method of lysing an endosome, the method comprising the steps of:

providing a composition for endosomal uptake into the cell; and

contacting the composition with the cell in the presence of an endosomal lysing agent having one or more hydrozable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyls and wherein said agent is capable of effecting the lysis of an endosome in response to a change in pH.

Q6 SUB B7)

40. (Canceled)

41. The method of claim 39, wherein said endosomal lysing agent comprises a compound having one or more hydrolyzable functionalities and one or more ionizable functionalities.

42. (Amended) A method for introducing a nucleic acid into a cell or a subcellular component, the method comprising the steps of:

Q7 SUB B8)

providing a biocompatible delivery composition comprising:

a packaging agent;

an endosomal lysing agent having one or more hydrozable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyls and wherein said agent is capable of effecting the lysis of an endosome in response to a change in pH; and

a nucleic acid; and

contacting the composition with cells.

43. (Canceled)

44. The method of claim 42, wherein said endosomolytic agent comprises a compound having one or more hydrolyzable functionalities and one or more ionizable functionalities.

45. The method of claim 42, further comprising contacting the composition with cells in the absence of a known endosomal lysing component selected from the group consisting of chloroquine, polyethyleneimine, fusogenic peptides, inactivated adenoviruses and combinations thereof.